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MUSCLE STRENGTH, POWER AND TORQUE DEFICITS IN CHILDREN WITH TYPE SS SICKLE CELL DISEASE

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Abstract

In African-American children aged 5 to 17 years with and without type SS sickle cell disease (SCD-SS), dominant hand maximal handgrip strength, peak power and plantar flexion isometric maximal voluntary contraction (MVC) torque were compared with adjustments for body size and composition. Children with SCD-SS (n=21; age, 11±1 y) compared with healthy control children (n=23; 10±1 y) did not differ by age, sex or maturation stage, but had significantly lower Z scores for height, weight, BMI, arm circumference, upper arm muscle area, and lean mass-for-height. Children with SCD-SS had significantly lower unadjusted handgrip strength (16±2 vs. 23±2 kg, P<0.01), peak power (1054±107 vs. 1488±169 W, P<0.04) and MVC torques at two angles (10°: 27±3 vs. 42±5; 20°: 21±3 vs. 34±4 Nm; all P < 0.05). Performance decrements persisted when handgrip strength was adjusted for lean body mass and fat mass explaining 66% of the variance; peak power adjusted for age, lean body mass, fat mass and height explaining 91% of the variance; and the highest MVC torque (10° angle) adjusted for left leg length, lean- and fat mass-for-height Z scores explaining 65% of the variance. This suggests additional factors contribute to the attenuated anaerobic performance.

Keywords

Pediatrics; Muscle Function; Biodex; Sickle Cell Disease; Muscle Torque

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INTRODUCTION

Throughout childhood, developing adequate muscle function is important for overall health, play activity and for rapid movement in emergency situations. Activities of daily living often require repeated bouts of anaerobic activity such as climbing the stairs or sprinting to catch a person or object. Additionally, children at play frequently engage in short bursts of high intensity exercise. Thus, anaerobic activity patterns are of practical importance to a child's daily life.

Previously, maximal muscle strength (by handgrip dynamometer) and peak power (by force plate) adjusted for body size and composition deficits were shown to be attenuated in children with type SS sickle cell disease (SCD-SS) compared to healthy African-American children¹. However, no study in this population has investigated if these muscle performance deficits persist using a more functional measure, muscle torque, defined as force applied over a distance causing rotation about a fulcrum. As a foundation of human movement, measurement of muscle torque provides an integrated assessment, as almost all movement generates torque to varying degrees. Additionally, in the current SCD clinical care environment, where the population of people with SCD may be upwards of 100,000 in the United States², hydroxyurea is considered a standard of care treatment and is prescribed at a young age. It is unclear if hydroxyurea use or other changes in treatment over the last decade may have reversed these body size and muscle performance deficits.

The purpose of this study was to compare dominant hand maximum handgrip strength, peak power and plantar flexion isometric maximal voluntary contraction (MVC) torque, adjusted for body size and composition, in a contemporary sample of 5- to 17-yr-old African-American children with and without SCD-SS. It was hypothesized that despite introducing hydroxyurea therapy at a younger age, children with SCD-SS have significantly reduced muscle strength, peak power and plantar flexor MVC torques after adjustment for confounding variables such as body size and composition compared to healthy children.

METHODS

Subjects

This was a secondary analysis of a randomized trial and the primary outcome and methods have been previously reported in detail³. Briefly, African-American children aged 5 to 17 years with and without SCD-SS were recruited for a vitamin D supplementation study. The baseline data (before vitamin D supplementation) were used for this analysis. Children with SCD-SS were recruited from the Comprehensive Sickle Cell Center at the Children's Hospital of Philadelphia (CHOP). Healthy subjects were recruited from the CHOP network of primary care centers and the greater Philadelphia region. Exclusion criteria for both groups included: participation in another study impacting 25 hydroxyvitamin D (25(OH)D); pregnant or lactating females; other chronic conditions or use of medications affecting growth, dietary intake, or nutritional status; use of vitamin D to treat vitamin D deficiency; and baseline elevated serum calcium concentration. Subjects taking supplements containing vitamin D were not eligible. Those willing to discontinue supplementation with approval of their medical provider were eligible after a two-month washout period. Additional exclusion

criterion for subjects with SCD were chronic transfusion therapy and for healthy subjects were body mass index (BMI) >85th percentile for age and sex⁴.

This protocol was approved by the Institutional Review Board at CHOP. Written informed consent was obtained from parents/legal guardians of subjects <18 years. Verbal assent was obtained from subjects 6 to <18 years.

Anthropometry and Pubertal Status

Anthropometric measurements were obtained in triplicate per standardized techniques⁵ and the mean used for analysis. BMI was calculated (kg/m^2) from weight using a digital scale (Scaletronix, White Plains, NY) and standing height using a stadiometer (Holtain, Crymch, United Kingdom). Weight, height and BMI were compared to reference standards to generate age- and sex-specific Z scores⁴, which is a measure of how many standard deviations below or above the population mean a measurement is located. Sixty-eight percent of normally distributed data are within one standard deviation of the mean (between -1 and 1), 95% are within two standard deviations, and 99.7% are within three standard deviation units of the mean. Skinfold thickness was measured at the triceps and subscapular sites with a skinfold caliper (Holtain) to estimate subcutaneous fat stores using prediction equations adapted for children and adolescents^{6,7}. Mid-upper arm circumference and triceps skinfold thickness measures were used to calculate upper arm muscle area (UAMA) and upper arm fat area⁸. These areas were compared with reference data from the National Center for Health Statistics to generate the Z scores⁹. Total body fat and lean body mass were measured using whole body dual energy x-ray absorptiometry (DXA; Delphi A, Hologic, Inc., Bedford, MA) and compared with the Reference Project on Skeletal Development in Children data to generate race- and sex-specific DXA Z scores for lean body mass (LBM-for-height) and fat mass relative to height¹⁰. At baseline, pubertal status according to the criteria of Tanner¹¹ was determined using a validated self-assessment questionnaire¹². Children were categorized into three groups for pre- to early puberty (Tanner stages 1 or 2), mid-puberty (stage 3) or late-puberty (stages 4 or 5).

Biochemistry and Hematology

Serum 25(OH)D was determined using liquid chromatography tandem mass spectrometry (Clinical Laboratory, CHOP, [CHOP]) with intra and inter assay coefficients of variation (CV) below 7%. Hematologic status was assessed by complete blood count (CBC: hemoglobin, hematocrit, mean corpuscular hemoglobin [MCH], MCH concentration, mean corpuscular volume [MCV], and red blood cell distribution width [RDW]) for all subjects and fetal hemoglobin was assessed in SCD-SS only according to standardized techniques. Serum high-sensitivity C-reactive protein (HS-CRP) was assessed in all subjects as an indicator of inflammatory status. Subjects with SCD-SS were categorized as receiving or not receiving hydroxyurea therapy during the study.

Muscle Performance

All subjects completed a 5-minute warm-up period of treadmill walking at a comfortable self-selected speed at 0% grade. Next, maximal handgrip strength of the right and left hand was measured in kilograms (kg) with a handgrip dynamometer (Takei Scientific Instruments

Co., Ltd., Tokyo, Japan). Hand dominance was determined by asking which hand was used to hold a pencil. The participants stood upright with the shoulder adducted holding the dynamometer, not touching the trunk. The handle was adjusted to the hand size of the child and no extraneous body movement was allowed during testing. For each hand, three maximal effort trials lasting 4-seconds to 5-seconds interspersed with 60-second rests were carried out (verbal encouragement provided) and the highest dominant hand value was retained for analysis.

Peak power in watts (W) was calculated from the force-time curve and velocity of the center of mass during a maximal vertical squat jump using a Kistler Quattro Jump Portable Force Plate System (Model 9290AD, Kistler Instrument Corporation, Amherst, NY). Participants completed three warm-ups followed by three maximal vertical jumps from an initial static squat position with knees at 90 degrees flexion and arms akimbo. The highest value was used for analysis^{13,14}.

Muscle torque was assessed using the Biodex Multi-Joint System 3 Pro (Biodex Medical Systems, Inc, Shirley, NY). High intrarater (0.97 to 0.99) and interrater (0.93 to 0.96) intraclass correlation coefficients have been reported for this method testing various body joints¹⁵. Prior to testing each subject was familiarized with the test procedures. Plantar flexion isometric MVC torques of the left ankle were measured in triplicate at each of four angles (−10, 0, 10, and 20 degrees) and the highest value in Newton meters (Nm) recorded for dorsiflexion and plantarflexion at each angle.

Statistical Analyses

All variables were tested for normality, and nonparametric tests were used as appropriate. Group differences were determined by using a Student's t test or Wilcoxon's rank-sum test for continuous variables and Fisher's exact or chi-square test for categorical variables. To assess potential group differences in muscle performance adjusted for age, and body size and composition, multivariate regression models were constructed using a multistage approach. Variables related to age, sex, body size, body composition, vitamin D, hematology and inflammatory status were explored, as was whether using or not prescribed hydroxyurea therapy. Selection of variables for final models was based on statistical significance, maximum R^2 values, and distribution of residuals. All statistical analyses were performed by using STATA 14.0 (Stata Corp, College Station, TX). Results were considered significant at $P < 0.05$, and data presented as means $\pm$ SD.

RESULTS

Characteristics of subjects are presented in Table 1. Twenty-one children with SCD-SS and 23 healthy control children did not differ by age, sex or maturation stage. Children with SCD-SS compared to healthy controls had significantly lower Z scores (all $P < 0.05$) for height, weight, BMI, arm circumference, UAMA, and whole body LBM-for-height. Hematocrit and hemoglobin were significantly lower and high-sensitivity C-reactive protein, MCH, MCV and RDW were significantly higher in children with SCD-SS vs. healthy control children.

For those treated vs. not treated with hydroxyurea therapy in the SCD-SS group, although there were no significant differences (all $P > 0.05$) in age (11 ± 4 vs. 11 ± 4), LBM-for-height Z score (-1.6 ± 1.2 vs. -2.1 ± 0.8), or fat mass for height Z score (0.5 ± 0.6 vs. 0.01 ± 0.6), there were significant differences (all $P < 0.05$) in the following body composition variables: height Z score (0.1 ± 0.9 vs. -0.9 ± 1.1), weight Z score (0.2 ± 0.8 vs. -1.2 ± 1.1), BMI Z score (0.04 ± 1.1 vs. -1.0 ± 0.9), arm circumference Z score (-0.1 ± 1.1 vs. -1.5 ± 0.9) and UAMA Z score (0.2 ± 0.4 vs. -1.2 ± 0.9).

Unadjusted dominant hand maximum handgrip strength ($P < 0.01$) and peak power ($P < 0.04$) were significantly reduced in children with SCD-SS compared to healthy controls (Figure 1). Using multiple regression analysis, a performance decrement persisted in dominant hand maximal handgrip strength (-4 kg) after adjusting for lean body mass and fat mass that together explained 66% of the variance (Table 2; lean body mass alone explained 65% of the variance). A deficit of 189.9 W persisted for peak power adjusted for age, lean body mass, fat mass and height explaining 91% of the variance (Table 3; lean body mass alone explained 89% of the variance).

Unadjusted MVC torques were significantly lower in children with SCD-SS compared to healthy subjects at two angles (both $P < 0.05$, Figure 1). The deficit for subjects with SCD-SS persisted (-7.3 Nm) when the highest MVC torques (at 10° angle) were adjusted for left leg length, lean- and fat mass-for-height Z scores using multiple regression, together explaining 65% of the variance (Table 4; left leg length alone explained 58% of the variance).

Hematologic and inflammatory status did not contribute significantly to the multiple regression models predicting any measure of muscle performance, and there were no differences found in performance by hydroxyurea use group (results not shown).

DISCUSSION

African-American children with SCD-SS compared to healthy African-American children of similar age and pubertal status had performance decrements in dominant hand maximum handgrip strength, peak power and plantar flexion isometric MVC torques. When measures were adjusted for body size and composition deficits, group differences were still evident. This underscores the importance of improving growth, body composition, and nutritional status in children with SCD-SS and suggests additional factors intrinsic and/or extrinsic to muscle tissue contributed to the reduced anaerobic performance. A previous study reporting that feeding a high-protein diet to transgenic sickle mice improved body composition and grip strength¹⁶ provides direction for future studies.

Strength and power deficits have been shown in children with SCD-SS^{1,17}. Findings from the present study agree with and extend previous work to show in a contemporary group of children with SCD-SS with almost half (9/21; 43%) taking hydroxyurea, body-habitus adjusted strength and power deficits were still present. Perna et al¹⁸ using data from the 2011-2012 National Health and Nutrition Examination Study (NHANES) published nationally representative combined handgrip strength means and percentile distribution in

US children by sex and age group. The maximal value from three trials per hand was summed to yield combined handgrip strength in pounds. We calculated combined handgrip strength in pounds from the present study for children with and without SCD-SS and compared to the means and percentile distribution by sex and age group from Perna et al¹⁸. Results, presented in Table 5 show that the children with SCD-SS consistently have a higher percentage in the lower percentile of the distribution of handgrip strength than healthy children. This is particularly evident in boys with 2/3 below the NHANES 20th percentile and 3/4 below the 50th percentile. Boys with SCD have previously been shown to have particularly large deficits in lean body mass, and these deficits increase through adolescence¹⁹. This supports findings from the present study suggesting strength deficits in children with SCD-SS. No study to date has assessed muscle torque in this population. We found reduced muscle torque, regardless of adjustment for commonly shown deficits in body size and composition in this group. Taken together, these performance deficits may result from factors intrinsic and/or extrinsic to the muscle, or by other yet to be elucidated factors.

Of the few exercise studies comparing children with SCD-SS to healthy children, the majority focused on aerobic performance. During an exhaustive cycle ergometer graded exercise test, work capacity, ejection fraction, and maximal cardiac output, heart rate and blood pressure were lower in children with SCD-SS compared to healthy children^{20,21}. To compensate for decreased oxygen-carrying capacity, children with SCD-SS extracted more oxygen resulting in a greater venous desaturation²² and displayed an exaggerated ventilatory response partially due to increased physiological dead space during steady-state cycle ergometer exercise at 50% of their maximal workload²³. Collectively these studies suggest a deficient cardiopulmonary response to aerobic exercise in children with SCD-SS compared to healthy children. These findings have significance as regular, moderate aerobic exercise is considered a good predictor of positive health outcomes in the general population. However, children's physical activity patterns are characterized by short bouts of high intensity motion, requiring instantaneous energy release from intramuscular high-energy phosphates. Since children engage in short-burst exertion when encouraged to be physically active, this form of movement should be part of assessments and targets to increase physical activity and quality of life in children. Anaerobic activity promotes muscle and bone development and thus is important for normal child development and lifelong health. However, there is a paucity of empirically-based information comparing anaerobic exercise performance between children with SCD-SS and healthy children. In this study, the three measures used to evaluate anaerobic performance were all lower in children with SCD-SS vs. healthy African American children. Factors possibly contributing to these deficits will be outlined below.

Using a mouse model stimulation protocol, muscle mass independent maximal tetanic force and peak force were reduced in SCD-SS vs. control mice²⁴. It was suggested that SCD associated oxidative stress reduces myofibrillar calcium sensitivity resulting in impaired calcium uptake by the sarcoplasmic reticulum, leading to impaired muscle function. The same authors showed increase intramuscular acidosis and a depletion of phosphocreatine (PCr) concentration in addition to higher glycolytic enzyme activity during exercise in SCD-SS vs. control mice²⁵. It was speculated that the increased glycolytic contribution to adenosine triphosphate production was associated with hydrogen ion accumulation which

has been shown to disrupt muscle function²⁶. Additionally, the faster depletion of PCr stores suggests perturbations in oxygen supply. These likely result from the commonly known SCD complications of chronic hemolytic anemia and arterial desaturation, or from low capillary density and tortuosity²⁷ or lower microvascular muscle oxygenation²⁸ in SCD. Deep tissue hyperalgesia has been proposed as an additional hypothesis contributing to muscle dysfunction given that analgesia improved muscle strength in SCD mice²⁹. Via muscle biopsy of the vastus lateralis muscle, changes in fiber type distribution were observed in adults with SCD vs. healthy adults (average age 23 to 25 yrs) with a higher proportion of type I and a lower proportion of type IIa muscle fibers²⁷. Some adults with SCD had intercellular adipocytes indicative of muscle degeneration suggestive of muscle wasting. Also found were muscle atrophy, higher satellite cell number, and decreased activity of creatine kinase and several oxidative enzymes in adults with SCD vs. controls. Any of these intramuscular factors alone or in combination could have contributed to the performance decrements observed in the present study. In addition, there are potential factors extrinsic to muscle that may also play a role and these will be outlined below.

In both children and adults with SCD-SS, autonomic nervous system impairment has been shown characterized by parasympathetic withdrawal and sympathetic predominance³⁰⁻³². Although exercise is associated with autonomic nervous system activation via parasympathetic withdrawal and increased sympathetic activity, few studies have assessed if the sympatho-vagal imbalance present in SCD-SS might affect aerobic and/or anaerobic exercise performance. Alvarado et al³³ assessed autonomic system dysfunction by heart rate recovery after a maximal exercise test in subjects with SCD-SS ages 8 to 21 years. Results showed reduced heart rate recovery post exercise suggesting parasympathetic dysfunction and that the impairment becomes worse with age. In adults with SCD-SS, Martins et al³⁴ found no difference in the blood pressure or heart rate response to a maximal dominant handgrip strength test whereby the subject maintained 40% of maximal strength for 90 seconds. However, these authors also showed that in response to three conditions (the valsalva maneuver, diving maneuver, and tilt test), cardiovascular autonomic dysfunction was present characterized by reduced baroreflex sensitivity and limited heart rate regulation via the parasympathetic nervous system.

Subclinical peripheral nerve involvement is an area of recent focus in SCD. In one study, the frequency of peripheral neuropathy was assessed in 51 children and adults with SCD-SS aged 15 to 51 years who had no clinically evident neurological signs and symptoms³⁵. Peripheral nervous system involvement was observed in 20% of subjects including nerve conduction abnormalities, demyelination and axonal degeneration. However, at the time of the nerve conduction assessments, 35 subjects were on hydroxyurea, 6 were on transfusion therapy and 10 were not on specific SCD treatment. Electrophysiological studies of peripheral nerves are not routinely conducted in patients without clinical symptoms and thus the overall prevalence of subclinical peripheral nerve involvement in SCD is not well understood. Another possible factor could be that those with SCD-SS have a lower percentage of voluntary activation which could explain, at least in part, the lower muscle force production³⁶ and future studies should investigate this hypothesis.

In the clinical setting, empirical assessment of muscle performance, utilizing standardized protocols for reproducibility, is important for evaluation and treatment. Objective measures of muscle strength, power and torque enable the clinician to determine the patient's current functional status while also forming the basis upon which a program for rehabilitation can be prescribed. The novel finding in the present study of a reduction in MVC torques in children with SCD-SS vs. healthy controls provides a better understanding of deficits in anaerobic ability beyond what is learned from hand grip strength and peak power that can help to guide clinical care interventions in this population. Torque is defined as force applied over a distance (lever arm) causing rotation about a fulcrum (axis of rotation). Simply stated, torque is what creates and drives biomechanical movement. Muscle torque is important in clinical care because the ability to maximize the amount of torque a muscle can generate enables optimal strengthening of the muscle. If the goal of treatment is to facilitate movement, the torque variables can be manipulated to enhance muscle efficiency to move a body part. For example, previous exercise intervention studies have demonstrated improvements in the torque-angle relationship at the shoulder joint in young healthy subjects³⁷ and male soccer players³⁸. Another study showing deficits in muscle torque in the 60 years and older group suggested including weight training or strength-endurance training to improve overall daily functioning³⁹. Future research should investigate the efficacy of these and other exercise interventions to reverse MVC torque deficits in SCD-SS and should include patient-reported outcomes representation of these domains of physical function and quality of life.

Previously in children with SCD-SS peak power Z scores positively correlated with fetal hemoglobin (disease severity)¹. In the present study, hematologic or inflammatory status did not influence performance. A previous study conducted in SCD mice suggested that inflammatory status (at the muscle level) was not related to muscle dysfunction²⁴. It is unclear if sample size, age, sex, or other factor(s) contributed to these differences in findings from the previous study and more research is needed. We found no differences in performance when comparing those treated vs. not treated with hydroxyurea therapy in the SCD-SS group, on hydroxyurea therapy in the SCD-SS group vs. controls, or when all three groups were compared (SCD-SS on hydroxyurea, SCD-SS not on hydroxyurea and controls). Interestingly, for those treated vs. not treated with hydroxyurea therapy in the SCD-SS group, although there were no significant differences in age, LBM-for-height Z score, or fat mass relative to height Z score, there were significant differences in height Z score, weight Z score, BMI Z score, arm circumference Z score and UAMA Z score. It is unclear if the lack of an effect of hydroxyurea on performance could be attributed to sample size limitations, possible lack of changes in lean body or fat mass due to such a short study duration, variability in adherence to hydroxyurea, age, sex or other factors and more research is warranted.

A limitation of the present study is that level of physical activity related to frequency, intensity or duration was not assessed. It has been previously suggested that the low physical activity level of patients with SCD could play a role in muscle repercussions related to remodeling of the microvascular, structural, and energetic characteristics of skeletal muscle²⁷. Future research to assess the impact of low physical activity level on muscle perturbations in SCD is indicated.

In conclusion, after adjusting for growth and body composition deficits, maximal muscle strength, peak power and MVC torques were reduced in children with SCD-SS compared with healthy control children. This suggests that additional factors contribute to attenuation in anaerobic performance.

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Figure 1.

Boxplots showing that unadjusted values for dominant hand maximum handgrip strength (A), peak power (B), and plantar flexion isometric maximal voluntary contraction (MVC) torques at angles 10° (C) and 20° (D) were significantly reduced in children with SCD-SS compared to healthy controls (all $P > 0.05$). The top, bottom, and line through the middle of the box correspond to the 75th percentile (top quartile), 25th percentile (bottom quartile), and 50th percentile (median), respectively. The whiskers on the bottom extend from the 10th percentile (bottom decile) and top 90th percentile (top decile). MVC, maximal voluntary contraction.

Table 1

Subject Characteristics

	SCD-SS ^a	Controls
N	21	23
Age (yr)	11 ± 4 ^b	10 ± 4
Sex (#)		
Male	9	13
Female	12	10
Tanner (#)		
1 or 2	14	13
3	3	5
4 or 5	4	5
Height Z score	-0.5 ± 1.2	0.4 ± 1.0 *
Weight Z score	-0.7 ± 1.2	0.8 ± 1.1 *
BMI Z score	-0.6 ± 1.1	0.7 ± 1.1 *
Arm circumference Z score	-0.9 ± 1.1	0.8 ± 1.6 *
UAMA Z score	-0.6 ± 1.2	1.0 ± 1.8 *
LBM-for-height Z score	-1.9 ± 1.0	-0.9 ± 1.4 *
Hematocrit (%)	25.9 ± 3.1	39.8 ± 3.1 *
Hemoglobin (g/dL)	8.4 ± 1.0	13.0 ± 1.1 *
Fetal Hemoglobin (%)	12.4 ± 5.8	
HS-CRP (mg/L)	3.0 ± 2.6	1.1 ± 1.5 *
MCH (pg)	30.1 ± 3.4	27.2 ± 2.1 *
MCHC (g/dL)	32.4 ± 1.0	32.7 ± 1.1
MCV (fL)	92.7 ± 9.2	83.0 ± 5.5 *
RDW (%)	20.0 ± 2.5	13.3 ± 1.1 *
Total 25(OH)D (ng/mL)	19.2 ± 7.2	22.3 ± 9.3
On hydroxyurea (#, %)	9 [43]	

^aSCD-SS, type SS sickle cell disease; BMI, body mass index; UAMA, upper arm muscle area; LBM, lean body mass; HS-CRP, high-sensitivity C-reactive protein; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RDW, red cell distribution width; 25(OH)D, 25 hydroxyvitamin D.

^bMean ± SD (all such values).

* P<0.05, SCD-SS vs. Controls.

Table 2
Multiple Regression Model Predicting Dominant Hand Maximum Handgrip Strength

	Coefficient (kg)	Standard error	t	P-value	R ²
All (n = 44)					0.66*
SCD Group	-4.0	1.8	-2.2	0.032	
LBM, kg	0.7	0.1	6.7	0.001	
FM, kg	-0.2	0.2	-1.4	0.160	
Constant	8.4	3.8	2.2	0.033	

SCD, sickle cell disease; LBM, lean body mass; FM, fat mass.

* Lean body mass explained 65% of the variance.

Table 3**Multiple Regression Model Predicting Peak Power**

	Coefficient (W)	Standard error	t	P-value	R²
All (n = 44)					0.91 *
SCD Group	-189.9	75.6	-2.5	0.017	
Age, yr	74.2	23.5	3.2	0.003	
LBM, kg	73.7	9.5	7.8	0.001	
FM, kg	-6.5	6.5	-1.0	0.325	
Height, cm	-22.9	6.6	-3.5	0.001	
Constant	2058.5	598.5	3.4	0.001	

SCD, sickle cell disease; LBM, lean body mass; FM, fat mass.

* Lean body mass explained 89% of the variance.

Table 4

Multiple Regression Model Predicting Highest (at 10° angle) MVC Torque

	Coefficient (Nm)	Standard error	t	P-value	R ²
All (n = 44)					0.65 [*]
SCD Group	-7.3	3.3	-2.2	0.033	
LL Length, cm	1.8	0.3	5.5	0.001	
FM-for-height Z score	2.8	2.7	1.0	0.303	
LBM-for-height Z score	1.6	1.8	0.9	0.368	
Constant	-22.7	14.0	-1.6	0.112	

MVC, maximal voluntary contraction; SCD, sickle cell disease; LL, Length, left leg length; FM, fat mass; LBM, lean body mass.

^{*} Left leg length explained 58% of the variance.

Table 5

Comparison of Combined* Grip Strength (Pounds) From Present Study to Mean and Percentile Distribution by Sex and Age Group from 2011–2012 NHANES^a (Perna et al., 2016)

	% <20		% <50	
	SCD-SS	Controls	SCD-SS	Controls
Males	67	29	78	57
Females	42	30	67	50

* Maximal value from each hand (3 trials each) was summed to yield combined grip strength (pound)

^aNHANES, National Health and Nutrition Examination Survey; SCD-SS, type SS sickle cell disease

Note: sample sizes are 9 and 12 in SCD-SS sample and 13 and 10 in control sample for males and females, respectively.